

MORTALITY AND MORBIDITY FOLLOWING KIDNEY
TRANSPLANTATION: PREDICTIVE UTILITY OF PSYCHOLOGICAL
VARIABLES

By

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Abstract of Dissertation Presented to the Graduate School of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

MORTALITY AND MORBIDITY FOLLOWING BONE MARROW TRANSPLANTATION: PREDICTIVE USEFULITY OF PSYCHOLOGICAL VARIABLES

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Bone marrow transplantation (BMT) is a treatment for a wide range of hematologic, immunologic, metabolic and neoplastic diseases. Until recently, studies investigating BMT outcomes focused primarily on medical variables, such as graft-versus-host disease and the effect of T cell depleted marrow on relapse. Recently, however, several studies have investigated the impact of psychological variables on BMT outcomes. These studies have investigated the impact of depression, anxiety, family support, quality-of life and personality on survival after BMT. Overall, these studies have reported mixed results suggesting that depression, anxiety, perceived family support, and personality may have some impact on survival time after BMT.

The purpose of the current study was to explicitly investigate the predictive

study of psychological variables (effect, social support, post-transplant history) on RMT outcomes (current time physical functioning and quality of life) (pre-RMT). Patients were assessed retrospectively by two independent examiners to rate their levels of pre-RMT social support, effect and transplant history. Subjects were then assessed post-RMT to measure their quality of life, symptom report and survival time. Results of the study suggested that pre-RMT psychological variables were linked to outcomes in terms of both mortality and psychological morbidity. People with higher levels of anxiety and depression pre-transplant were more likely to report poorer perceptions of physical health, increased frequency of symptoms and increased distress about those symptoms post-transplant. People with lower levels of social support appear to be at increased risk for morbidity compared with those with adequate social support. However, social support may cause individuals to focus on their symptoms more than they otherwise would and to decrease their unmet physical needs. Individuals with higher levels of social support reported more frequent symptoms and more distress about those symptoms than did individuals with lower levels of social support. The results of the study will be useful in helping identify those potentially patients at risk for negative outcomes to RMT and in developing interventions to aid patients at high risk. The implications and limitations of the study, as well as future research directions, are discussed.

CHAPTER 1 INTRODUCTION

Bone marrow transplantation (BMT) is a treatment for a wide range of hematologic disorders, including leukemia and myelodysplastic diseases. While the concept of bone marrow transplantation dates back to the 1920s, not until the 1970s did rapid clinical progress occur. By the 1990s, BMT had emerged as a treatment with some degree of success in curing various life-threatening diseases, cancer, aplastic anemia and leukemia (Tedesco & Harris, 1993). Bone marrow transplantation refers to five specific procedures: (1) syngeneic transplantation, in which the bone marrow of a genetically identical twin is transplanted; (2) allogeneic transplantation, in which marrow from a related or unrelated donor is used; (3) autologous, in which the patient's own bone marrow is cryogenically preserved and reintroduced into the patient's system; (4) umbilical transplantation, in which stem cells are extracted from bone marrow or peripheral blood and cultured before re-implant; and (5) cord blood transplantation, in which stem cells are taken from umbilical cord blood supply, cultured and re-implanted. However, for simplicity these procedures will be grouped together under the general term bone marrow transplantation. BMT typically occurs as part with regimen of total body irradiation and chemotherapy.

Until recently, studies investigating BMT processes focused primarily on medical variables, such as graft versus-leuk disease (GVLD) (Brunner et al., 1997) cited as

Talbot & Brown, 1982), the effect of T cell depleted marrow on antigen (alloreactive) *et al.*, 1986, cited in Campbell, 1990 (Fisch *et al.*, 1985, cited in Campbell, 1990) and the impact of immunosuppression on survival in BMT patients (Flynn, Flinnsey, & Thomas, 1988, cited in Campbell, 1990). However, several recent studies have investigated the impact of psychosocial variables on BMT outcomes. These studies have investigated the impact of depression, anxiety, family support, quality of life, and personality on survival after BMT (Antipinovich, Brady, & Merzian-Gervey, 1984; Cohen, Cohen, Popovich, McKinn, 1988; Meyer, 1988). Overall, these studies have reported mixed results suggesting that depression, anxiety, perceived family support, and personality may have little impact on outcomes after BMT.

The current study was an attempt to empirically investigate the predictive validity of psychosocial variables on BMT outcome (survival time, physical functioning, and quality of life post-BMT). At the University of North Health Science Center, BMT patients are routinely evaluated using clinical interviews and standardized psychological measures as part of their pre-transplant screening. Psychosocial factors are considered in the same manner when medical factors are used. (1) It seems that physical benefits outweigh the risks to the patient, and (2) to really address a patient's concerns (Birnack & Lapanian, 1989). These psychological variables are transformed into composite scores reflecting patients' adaptation along various psychological dimensions. The utility of these pre-transplant psychological dimensions in predicting mortality and morbidity post-BMT was

investigated. For BMT patients still living, the composite measured to predict physical functioning and quality of life. Quality of life and physical functioning were assessed using a standardized health-related quality of life (HRQL) instrument, a BMT-specific QOL measure, and a symptom checklist. The results of this study will hopefully be useful in assessing transplant status in developing interventions to aid patients at high risk for negative outcomes of BMT. In the future research section below, control areas will be briefly covered: a description of the history and procedural aspects of BMT will be given, the influence of psychological factors on autologous/progenitor variables will be reviewed, the impact of psychological factors on BMT outcome will be investigated, and quality of life in adult medical and BMT populations will be covered.

CHAPTER 1 REVIEW OF THE LITERATURE

History

Bone marrow transplantation is a procedure which gained widespread acceptance in the 1950s as a highly expected treatment for a variety of disorders. The first BMT was attempted in 1956 when bone marrow was administered orally to cases of defective blood formation. Tishler and Barret (1956) stated that there was no problem after these first transplants because there was no possibility of transferring living cells through oral administration. In 1956, Schurwenger (cited in Tishler & Barret, 1956) administered intravenous injections of bone marrow to cancer patients, and had some positive results due to the transfer of living cells. In 1956, Larson (cited in Tishler & Barret, 1956) established that marrow transplants could correct bone marrow failure syndromes, and could protect patients against the effects of radiation and chemotherapy. Thus began modern research on allogeneic and autologous BMT.

During the 1950s and 1960s much research was done on a variety of important variables in BMT. For instance, graft versus host disease (GVHD) was first described during this time (Jelliffe et al., 1957; and in Tishler & Barret, 1956). GVHD is a fairly common syndrome in allogeneic transplants in which the newly infused marrow recognizes the host tissues as foreign and begins to attack the patient's immune system. Another important medical advance was Damesha et al. (1961) cited in Tishler &

French, 1993) description of the human leukocyte antigen (HLA) system. This discovery led to the development for bone marrow matching, thereby increasing the success rate of allogeneic grafts.

The 1990s saw a tremendous expansion in the use of BMT worldwide. One, undoubtedly key reason of BMT results to the increased bone marrow Transplant Registry in Minnesota has made statistical analysis of large patient groups possible. Recently, there has been increasing interest in studying diseases for allogeneic BMT other than HLA-related diseases, including matched but unrelated donors (Pearson et al., 1993) cited in Table 1 and French, 1993). There also has been research investigating, independent of "graft" or not the patient's manner of acquiring leukemia cells before a transplantation, allogeneic transplants. This procedure shows promise in decreasing the rate of relapse (Laporte et al., 1993) and has been used mostly in patients with acute leukemia or lymphoma or chronic leukemia (Table 1, 1993, personal communication).

A relatively new area of investigation in BMT research is stem cell and specialized transplants. The hematopoietic stem cells are responsible for mature representation after BMT. Sufficient numbers of stem cells for transplantation can be obtained from the peripheral blood supply after patients, with chronic therapy or growth factors. Transplants can also be administered using cells obtained from cord blood at the time of delivery (Thomas, 1993). The blood is being typed and cryopreserved for later use. Given the general availability and ease of procuring cord blood, this type of transplantation is a good

otherwise to hematopoiesis or peripheral blood cells as a source of transplantable tissue (Friedhelm et al., 1977). Two advantages of cord blood transplantation are the source, allografts available donor and the seemingly improved rate of graft versus host disease (GVHD) compared to hematopoiesis or peripheral blood stem cell transplantation (Whitehead et al., 1996).

Description of Current BMT Procedures

As noted above, there are several types of bone marrow transplants: syngeneic, allogeneic, autologous, stem cell, and cord blood. Since the current study involves only patients receiving autologous, allogeneic and syngeneic transplants, these procedures only will be described further. The majority of allogeneic marrow transplants are for leukemia or other malignancies, but they also are performed on patients with aplastic anemia and other "bone marrow failure disorders" (Champlin, 1998). Autologous transplants usually are performed on patients with hematologic malignancies and solid tumors.

Allogeneic BMT differs from solid organ transplants in that bone marrow is not usually rejected due to cell lineage differences (immune allogeneic antigens) unless there is a rapid or massive double rejection (Champlin, 1998). While patient is not sufficiently immunosuppressed, graft rejection can occur. Conversely, graft versus host disease can occur if immune-competent cells in the donor marrow react against the host tissue (Antikarov et al., 1996). Graft rejection and GVHD are more common with marrow

genetic disparity between the donor and host marrow. Typically, BMT is accompanied by a conditioning regimen of high dose chemotherapy and total body irradiation (TBI).

Allogeneic BMT encompasses three types of grafts: haplocompatible, fully histoinert, and matched unrelated donor (MUD) grafts. These grafts differ both in the source of the marrow, and the extent of tissue match between the donor and host marrow. The extent of tissue match is based on the human leukocyte antigen (HLA) system. The antigens are inherited and encoded. HLA-compatible BMT involves transplantation of marrow that is completely HLA matched (i.e. HLA identical). Haploidentical BMT uses donor marrow that is only partially HLA matched (i.e. less than a 6 antigen match). BMT using an unrelated donor can be either haploidentical or histoincompatible. Matching risk can vary according to HLA mismatching, duration, severity and a host who is only affected by marrow (Andersson, Brada & Hensley-Dunaway, 1994).

Autologous BMT does not carry with it the problem of graft rejection and GVHD since the patient is infused with his or her own marrow. However, relapse is higher in patients receiving autologous transplantation (Seligson, 1991; personal communication). This is presumably due to the presence of disease cells in the cryopreserved marrow. New techniques have been developed for purging autologous bone marrow, but their clinical utility is still being evaluated (Seligson et al., 1994).

Following transplantation, there are three stages through which patients progress (Chompho, 1992). In stage 1, patients are immune-suppressed with a systemic regimen

that leaves them susceptible to infections from bacteria, viruses, and fungi. In Stage 2, redistribution to the marrow post-BMT protects at the highest rate of graft failure, acute GVHD, and infections from cytomegalovirus (CMV). In Stage 3, patients often are conditioned with chronic GVHD while constant threat of secondary malignancies and relapse. Champlin (1994) also notes that alterations in the immune system of BMT patients persist beyond the first post-BMT. However, most evidence of immune dysfunction involved by first post-transplant

Psychological Factors Involved in BMT

Not surprisingly, BMT places great demands on the emotional resources of patients, family members, and hospital staff. Some BMT patients exhibit anxiety, depression, withdrawal, anger, "survivor guilt," non-compliance with staff or with self care requirements, sleep difficulty, anorexia, and paranoia (Giedyczynska, 1990). Some have suggested that all BMT patients experience these symptoms to some degree or probably experience some during transplantation (DeWitt-Kelly, 1994). The relationship between these psychological symptoms and health outcomes (i.e., quality of life) has only recently been brought to

Colton, Cohen, Foglio, and MacLennan (1992) investigated the impact of depression and family support on survival post-BMT in 60 adult leukemia patients. In this study, retrospective chart review yielded non-objective measures of post-transplant depression and family support. Depression, family support, and number of infections from leukemia

were used to predict pre-transplant survival. The results yielded three findings: 1) patients who were depressed had poorer survival rates compared to non-depressed patients; 2) patients with low ratings of family support had poorer survival rates than patients with adequate family support; and 3) patients who were in their first remission from leukemia had improved survival rates compared to those in second remission or relapse. Although these findings provided some evidence for the predictive utility of psychosocial variables pre-transplantation, the study has several important limitations including the lack of a prospective design, and the absence of standardized rating scales to measure psychosocial variables such as depressive and family support.

In another study, Andrykowski, Brady, and Flordis-Duncan (1994) prospectively assessed depressive quality of life, survival, adjustment to cancer, demographic variables and medical variables in a sample of 42 adults with leukemia who were undergoing allogeneic transplantation. Results indicated that quality of life was the only variable that showed a significant correlation relationship with survival. Patients receiving a heterozygous graft survived longer than patients receiving a haploidentical or matched unrelated donor (MUD) graft. However, results were found for several psychosocial variables. Specifically, higher "cancer preoccupations" and greater functional quality of life pre-BMT were associated with shorter post-BMT survival. No other psychosocial variables (e.g., depression, anxiety) showed trend significance. The authors suggested

that the small sample size was likely responsible for their failure to show significant utility of psychosocial variables in predicting survival.

Georgiadis et al. (1994) administered the State-Trait Anxiety Inventory (Spielberger et al., 1990) to 23 patients during the first week of allogeneic BMT and again at the end of isolation from leukemia on flow. They were interested in exactly what possible predictors of acute GVHD (Stages II-IV). Patients were evaluated for signs of GVHD on days +28, +40 and +100 post transplant. The authors found that state and trait anxiety were both significantly elevated during week one of BMT in patients who subsequently developed acute GVHD. With respect to the outcomes of BMT and level of severity, only state anxiety during the first week of isolation was significantly higher in patients who subsequently died from a relapse. The authors concluded that anxiety may influence adversely and the development of GVHD through the action of cytokines, highlighting a role in connecting the neuroendocrine and immune systems.

Maciej (1993) examined the impact of personality on survival rates post-BMT in 11 adult patients with a variety of diagnoses. Patients were given a German language version of the Personality Research Form (PRF) within the first seven days after admission to the hospital. They found that variables "strongly for recognition and help" and predictors of post-BMT survival. Maciej (1993) suggests that this scale might be highly correlated with patient compliance (i.e. patients scoring highly on this scale are more compliant). In another study, Ogata et al. (1992) investigated the physical and

psychosocial functioning of 67 allogeneic BMT survivors for 4 years post-BMT. They found that a high level of family conflict pre-BMT was predictive of difficulty in physical and psychological functioning after transplantation.

Jenkins, Lester, Alexander, and Winkler (1994) examined the influence of psychosocial variables such as depression and anxiety on length of stay, survival post-BMT, and psychosocial adjustment post-BMT. Twenty-eight patients undergoing BMT (both allogeneic and autologous) completed self-report forms measuring anxiety and depression. They were followed up to 4 months post-discharge. The authors believe that a significant link between depression or anxiety and survival. Also, pre-BMT depression and anxiety were not associated with increased length of stay. However, psychosocial morbidity post-BMT was correlated with depression and anxiety pre-transplant. Specifically, depressed patients required greater degrees of assistance emotionally and psychologically post-BMT.

In a follow-up study Murphy, Jenkins & Winkler (1995) gathered data on 189-on patients using both structured diagnostic interviews as well as unstructured interviews. They then compared the mean survival of patients with and without depression. The authors found that the presence of depression demonstrated correlation with length of survival. In addition, the presence of 'fighting spirit' and predominant coping style did not correlate with survival. The authors suggest that survival may be more closely related to physical rather than psychosocial factors.

Leigh, Wilson, Burns & Clark (1995) cited as Dragarovic et al. (1994) prospectively assessed 31 BMT patients pre-transplant using measures of anxiety, depression and social adjustment. Patients were then reassessed using the same instruments at 4 and 8 months after BMT. Overall, 34% of their sample showed "psychosocial morbidity" defined as anxiety or depression in excess of normal populations on the measures used. Subjects who showed abnormally following BMT also tended to score abnormally pre-transplant, suggesting a predictive value of pre-BMT psychosocial assessment. In addition, psychological morbidity was correlated to type of transplant. Patients who had allogeneic autotransfer therapy prior to BMT showed higher scores of psychological morbidity than did patients who had not undergone major medical treatment prior to BMT. Finally, subjects who received psychotherapy following their diagnosis were less likely to have depression or anxiety at 4 or 8 months follow-up.

In summary, the question of whether psychosocial variables impact on morbidity and mortality in BMT patients has yet to be fully answered. While there have been mixed results in the area of inquiry, preliminary results suggest that psychosocial variables such as depression and anxiety may play a role in post-BMT morbidity and mortality. Theoretically, why should this be the case? Two lines of research, one investigating the role of psychological factors in the development of medical illness, and the other investigating the field of psychoneuroimmunology, provide theoretical support for the initial investigations.

Psychological Factors Involved in Development of Clinical Issues

A related area of study is the impact of psychological factors such as depression and personality on the development of medical diseases. While many studies have found links of varying significance between psychological factors and the development of cancer (Blomberg, West & Lillo, 1984; Finch, & Marshall, 1982; Fox, 1982) only one of the more well designed studies will be presented here.

Stokols *et al.* (1982) administered the Minnesota Multiphasic Personality Inventory (MMPI) to a group of 1,167 male employees at Western Electric. The authors hypothesized that depression as measured by the MMPI would be associated with increased risk of death from cancer over a 17 year following period. Approximately 15% of these men were judged to be depressed and these men represented a carefully matched set of male death from cancer over the next 17 years. The authors controlled for age, cigarette smoking, EPOR consumption, family cancer history, and occupation. Both depressed and non depressed groups were similar on all of these factors. While considering statistical associations in the study the authors concluded that even though the magnitude of the correlations are similar to those observed between coronary heart disease and its major risk factors of high cholesterol, hypertension and cigarette smoking, death from cancer was not associated with any of the other standard scales of the MMPI.

Lofgren and Christensen (1982) published a study which directly replicated that of Stokols *et al.* (1982). The authors administered the Center for Epidemiologic Studies

Depression Study (C33-C5) is a group of 3,394 subjects. These subjects were followed for 12 years post-test administration. The authors found no significant correlation between depressed mood and development of cancer, although there was a trend for depressed subjects to develop cancer more frequently than non-depressed subjects. However, following anKaplan-Meier analysis, the authors found large increases in cancer risk in depressed smokers, compared to their non-depressed, non-smoking peers.

In summary, these studies indicate that there is a correlation between negative affect and the development of cancer. However, a causal relationship has not been established, and the strength of the relationship is not exactly clear at the present time.

Influence of Psychological Factors on Immune System Function

Why have studies found correlations between psychological factors, development of medical illness, and survival? The relatively new field of psychoneuroimmunology may provide some answers. Psychoneuroimmunologists study the body's mind relationship as rational and healthy links. They posit that immunopsychological processes are capable of eliciting immune factors and that conversely, events that occur as part of immune responses should modulate behavior (Mason, Wolfson, & Flaker, 1994). There is an intimate link between the central nervous system (CNS) and the immune system (see Mason, Wolfson & Flaker, 1994 for a detailed review). The sympathetic nervous system innervates immune organs such as the thymus, bone marrow, spleen and lymph nodes. Also, the endocrine system that causes endocrine glands to secrete hormones acts on

secretion. This enables hormones to reach the various hormone-related organs and bind to hormone receptors on those organs. The hypothalamus is also integral to anterior pituitary, and can increase or decrease anterior pituitary.

Conditioned immunity refers to the capability of psychological events to alter immune function. There are two lines of research investigating conditioned immunity: classical conditioning of immunity (Smith & McEwen, 1982), and the impact of stress on immunity. Classically-conditioned immunity (e.g. pairing a taste with an immunosuppressive drug, not Anderson *et al.*) has been demonstrated in animals and humans, although it is unclear if this conditioned immunity is clinically significant in humans in the form of disease progression or cure. Rongning *et al.* (1992) found that women who had undergone chemotherapy displayed immunosuppression after simply being brought to the hospital prior to chemotherapy. Gendreau *et al.* (1991) suggested that conditioned immune-suppression could delay breast resection or even meaning breast transplantation.

The impact of stress on immune functioning has the lower limb of body stress has been found to activate the sympathetic nervous system and the hypothalamo-pituitary-adrenal (HPA) axis, which regulates immune functioning (Mayer, Wolkstein, & Fendler, 1994). In particular, anger, anxiety, and depression have all been found to decrease activities of immune functioning. Initial studies supported the observation that while

acute exposure to a stressor and suppress immune response, repeated exposure results in apoptosis and in some cases, reduced response (Brew, Keller, & Goldstein, 1999).

Recently, two comprehensive review articles have investigated the impact of depression on immunity. Stein et al. (2003) noted that "independent of reproductive alterations of decreased frequency of lymphocytes" were reported in depressed patients (Brewer, Weiss, 2002) and that "indices of immunocompetence are lower among the clinically depressed." A large-scale, meta-analytic study was conducted (Stein and Cohen (2005) in attempt to clarify the research in this area. The authors included evaluations of all published studies as well as separate analyses restricted to studies meeting methodological criteria. Thirty-five studies were included overall, and included both quantitative and functional measures of immune functioning. Quantitative measures consist of counting the number of immune cells or the number of antigens in a blood sample. Functional measures study how effectively immune cells are functioning.

Stein and Cohen (2005) suggest that, overall, experimental evidence across numerous relationships between depression and both quantitative and functional measures of immunity. Effect sizes in methodologically controlled studies ranged from moderate (-.24) to large (-.45). Two possible explanations for this correlation are suggested. First, depression is associated with activation of the HPA axis and the sympathetic nervous system. Activation of these pathways results in elevated serum levels of cortisol and catecholamines. Immune cells have receptors for these hormones, suggesting that these

increasingly it is held to increase morbidity. An alternative explanation is that depressed people typically sleep less, have poorer nutritional intake, and have fewer health promoting behaviours than non-depressed counterparts (Farbani & Cohen, 1997).

Overall, psychoneuroimmunology points that a bi-directional set of processes occur. Classical conditioning and stress can alter immune function, and, conversely immune reactions and products can feed back and modulate behaviour and psychological state. This serves as a theoretical basis for the impact of psychosocial variables on mortality and morbidity in a BMT population.

Quality of Life in a BMT Population

In addition to survival, health related quality-of-life is an important outcome variable in transplantation research. Quality of life is a concept which has many facets, and incorporates aspects of physical health, personal and occupational functioning, mobility, and feelings of personal distress and well-being (Aschley *et al.*, 1974). Health-related quality of life (HRQL) covers five categories of concepts including duration of life, independence, functional status, perception of health and social opportunities (Finkel & Deyo, 1997). Until recently, QOL has not been widely researched in BMT patients. Research has been devoted to investigating mortality and medical morbidity (e.g. GVHD) while the impact of HRQL on the long-term quality of life of an transplant has been ignored. However, as Shaw-Edgson and Finkel (1992) point out, even when life is prolonged, it is important to measure QOL because patients may

experienced treatment-related adverse effects. The RMT continues to require survival, it is important to be cognizant of QOL issues in order to establish the relative costs and benefits of the procedure.

There is considerable diversity in the evidence available regarding the impact. However, there are several broad subject areas. Cognitive and social functioning have been measured, at least employment status, participation in physical health, performance of daily activities and psychological and social adjustment. Research has focused on measuring the long-term QOL of RMT recipients, and also identifying pre-RMT variables that assessed the likelihood of post-RMT QOL (Antikarovsky, 1994).

Cognitive functioning has been examined in several studies. Antikarovsky et al. (1995) found that cognitive impairment such as slowed reaction time and difficulties in learning were common in post-RMT patients. Also, the impact of the cognitive dysfunction was correlated with degree of total body irradiation (TBI) received. Several studies have also identified cognitive dysfunction as a barrier RMT patients (Kaneva et al. 1992; Benfield et al. 1993).

Social dysfunction is also an area within the QOL literature which has been investigated. Social dysfunction is a common occurrence, with most respondents unable to function, women experiencing social dryness, and both sexes frequently experiencing isolation (Fox et al. 1991) due to the TBI and chemotherapy. Studies while small in number, suggest that greater than 50% of adult RMT recipients report increased social

status, enjoyment in activity following BMT (Jansuch et al., 1994; Marston et al., 1993; Voss et al., 1992; Wiggall et al., 1992)

Edgar et al. (1994) examined a range of quality-of-life variables in a population of 114 BMT survivors 6-10 months post-BMT and found that survivors showed a high degree of overall satisfaction with life. However, these survivors were less satisfied with their bodies, level of physical strength and ability to achieve social satisfaction. Lack of social support was predictive of anger and negative affect. Patients transplanted at a later age experienced decreased quality-of-life overall.

Other studies that have investigated a broad range of QOL variables in a BMT population have been small in scope (i.e. <10 patients) and have relied on standard health outcome measures. Andrykowski, Hershman-Ginsberg, and Finkel (1991) investigated psychological and physical functioning in 20 adults 3-21 months post-BMT. Compared to a normative cancer population, BMT patients experienced more social distress, and poorer QOL. Also, older patients (greater than age 40) reported poorer QOL and more social distress than younger patients.

Wolcott et al. (1993) investigated adaptation in patients greater than one year post-BMT. They reported that approximately 50% of their sample was 'doing well' with the other 50% reporting emotional distress, chronic physical symptoms, less self-esteem and low QOL. Berggren, Hershman and Swann (1991) studied 17 adults 1-5 years post-BMT. Approximately 50% of the sample reported physical complications, social

problems, satisfaction and failure to return to employment. However/On, the authors advise that the majority of patients report positive changes in personality and social relationships.

Harman, Campbell, and Hyde (1991) reported on the QOL in 11 patients two years post-BMT. They compared perceptions of physical health as well as psychological and role functioning to a matched sample of individuals/patients receiving chemotherapy only. BMT patients reported more problems with sexual and vocational functioning; however, they did not differ from chemotherapy patients in their perceptions of physical health and their levels of psychological distress. However, Lurie et al. (1992) found no differences between BMT and conventional chemotherapy groups with regard to sexual and psychological functioning. However, both groups report greater levels of distress relative to a normative healthy sample.

Lewis, Rastegar, and Walter (1994) compared QOL in 14 BMT recipients and 11 conventional chemotherapy patients. No differences were found between groups on any QOL measure. In addition, both groups reported generally good QOL compared to a normative healthy group.

Peters et al. (1993) measured physical and psychological functioning in a sample of 107 BMT survivors. Median survival time was 50 months (range 4-154). Current functioning varied considerably across patients. However, the authors found that 83% of patients reported satisfaction in their quality of life. Psychological distress (anxiety and depression) was present in 22% of patients. They found that quality of life, psychological

distress and occupational status improved with the passage of time, particularly within the first 3 years post-BMT. Lower QOL, older age at BMT, shorter time post-BMT, female gender and recipient were significant predictors of impaired QOL.

Finally, Baker (1992) studied 124 BMT patients 1-4 years post-transplant and assessed QOL. The vast majority of patients perceived their QOL to be acceptable, but when present, problems centered around physical health and employment. Recently, several studies have improved upon the above studies by increasing sample size and including standardized, reliable measures of outcomes and QOL. Andrykowski et al. (1990) assessed a variety of QOL domains in BMT and renal transplant patients. Fifty-eight patients total were sampled. Overall, the group was comparable with another group reporting a "normal" QOL. Both groups experienced difficulty in sustained functioning, social relationships, and pain perceptions of physical health. QOL at T181 received during pre-BMT conditioning, and age at BMT were negatively correlated with current QOL.

Chen, Tierney, and Blumstein (1992) studied fifty-eight white leukemic BMT recipients at 10 days and 12 months post-BMT. They found that patients' ratings of QOL significantly improved between 10 days and 12 months. Fifty-eight percent of patients at 12 months reported above average or excellent QOL. In addition, TPA were employed and 47% considered their social functioning to be as satisfying as pre-BMT functioning.

In keeping with the observations, Schmidt et al. (1993) found that approximately 75% of patients in a sample of allogeneic BMT patients returned to work after 1 year post-BMT, while a majority reported sleep difficulties or sexual dysfunction. Whang et al. (1993) reported that perceived health, physical function, and social functioning were reported to be good or excellent for most patients in their sample of 155 BMT patients at least 5 months post-BMT. Approximately 75% of subjects were employed or enrolled in school. However, despite the strong reports of good functioning, some patients were still significantly impaired. Bone marrow was generally associated with greater life satisfaction. This finding regarding life satisfaction was replicated in another study (Blaker, Carlson & Nigam, 1993).

Examining the literature on QOL in a BMT population, it is apparent that post-BMT QOL varies considerably. A majority of patients report scores up to three average QOL indexes in normative healthy populations. There is little understanding regarding what factors predict the variability in QOL post-BMT. Demographically, younger patients seem to fare better after BMT. Research of value (e.g., level of knowledge, employment, bone marrow, etc.) has also been associated with greater life satisfaction. Among treatment variables, those of TBI have been linked to poor or usual, cognitive and physical functioning (Austyn et al., 1994). Very little is known regarding the impact of postulated psychosocial variables (i.e., affect, coping skills, social support) on post-BMT QOL or physical functioning.

Quality of Life: General vs. Disease-Specific Measurements

The present study is an attempt to determine the impact of psychological variables on general measures of QOL, and also derived from BMT. There is currently a debate in the literature regarding the measurement of QOL (Fady-Jermolovska, 1999). Controversy centers around whether to measure QOL on a disease-specific domain, or a "generic" QOL format. General health status measures are those that measure variables which are applicable across a wide range of illnesses. Disease-specific measures are those designed to assess specific patient populations, with the goal of measuring clinical change (Freckel & Eysa, 1999). The popularity of disease-specific measures is due to the clinical sensitivity of these scales. These scales are good for measuring changes that occur over time, and quantifying clinically important changes.

Four different models are relevant to examining the use of generic and disease-specific measures (Freckel & Eysa, 1999). The first approach is to include both generic and disease-specific measures in the same study even though the measures may overlap substantially. The second approach is to compare a generic measure and a generic instrument modified for the population of interest. However, there are no BMT modified instruments in the literature. The third approach is to use a generic health status instrument with a disease-specific instrument. This is similar to the first approach except that the disease-specific measure should have a different conceptual focus and

minimal overlap with the general measure. The further approach is to take a battery of specific measures which are scored independently and reported as individual scores.

The relative advantages and disadvantages of general and disease-specific measures depend primarily on the specific objectives of the study. IQQOL measures may be used to discriminate among respondents at a point in time, to predict future responses, or to measure change over time (Petack & Deyo, 1987). General measures typically have less disease validity because they contain items of little or no relevance to particular patient groups. By contrast, disease specific measures have high content validity for studies of particular patient populations. However, general measures have greater construct validity than disease-specific measures. Validity at a related time or which general measures has better than disease-specific instruments. There are few comparative studies of the test-retest reliability of disease-specific measures versus that of general measures (Petack & Deyo, 1987). In summary, general measures are well standardized, but disease-specific measures have the advantage of ease of administration, and good applicability to a specific population. Also, disease specific measures are useful in identifying important outcome alterations with particular conditions, and for measuring small clinically important changes in specific groups.

Aschmann (1988) suggests that it is important to measure both general and population specific aspects of QOL in a RCT population. He notes several weaknesses including the (1)–(4) Health Survey (Ware & Sherbourne, 1992), the Indiana Impact

Profile/Rosner, 1983b; Carter & Cohen, 1993; the FIM/F-6 (Cobb, Taitel & Day, 1992), and the Functional Living Index-Career (Rodriguez-Clark, McElroy & Lynn, 1994), which are appropriate for assessing QOL in a RCT population. The first two instruments are appropriate for all adult RCT recipients while the latter two are appropriate for all RCT recipients with adequate vision.

Other relevant lived above include the Spitzer Impact Profile (SIP) and the SF-36 Health Survey. The SIP is a measure which provides a profile of scores for different components of HRQL. The SIP measure includes related dysfunction in 12 different categories, producing 1 score for each category (Rosner et al., 1992). The SF-36 Health Survey (Rowe, Day, & Ware, 1988) covers a wide spectrum of health concepts for use in general medical populations. Both the SIP and the SF-36 have been tested extensively in a wide variety of patient populations and are well standardized for a range of patient populations, see Patrick & Day (1994). MacKinnon and Pettko (1992) suggest that while there is no obvious reason regarding what the 'best' QOL instrument for use in cancer populations, the SF-36 questionnaire is preferred, reliable, and valid for a wide range of medical populations.

Relevant quality HRQL measures for a cancer population include the Karnofsky Performance Status Scale for cancer (Karnofsky & Burchenal, 1949), the Quality of Life Index (QLI) (Folch, Lefkowitz, & Morris, 1984) and the Functional Living Index-Career (Rosner, Delmon, & Hall, 1992); the European Organization for Research and Treatment

of Cancer Quality of Life (American, et al, 1993) the Cancer Rehabilitation Evaluation System-Brief Form (CARES-BF) (Feling, Goss & Hatcher, 1993) and the Functional Assessment of Cancer Therapy scale (FACT-G) (Cella, et al, 1993).

Forcell et al. (1995) assessed QOL in a BMT population using an instrument termed the BMT Quality of Life Survey (BMT-QOL). The questionnaire instrument consisted of a one-item measure of EORTC summarizing its four-related questions. Content validity was established by a panel of BMT experts. Content analysis was performed on verbatim written responses to the six questions. The instrument yielded five domains of QOL in a BMT population: physical, psychological, social and spiritual well-being.

In a more methodologically rigorous study, Chan et al. (1995) developed a questionnaire for transplant BMT patients which addresses physical, psychological and functional well-being and treatment related side effects. The analysis included 14 subjects. The 14-item measure combined domain-specific symptoms specific measures of quality of life, and a global measure of QOL. They also included measures of social activity, work status, and perception of physical appearance. They found good reliability ($\alpha = .80$) in a randomly selected group of 20 patients administered the test twice.

Overall, the BMT specific QOL instruments currently available are unsatisfactory for use in the present study. More valid items measures for future strategy for assessing transplanters they gather use an overall QOL rating. This limits their ability

to be analyzed statistically. As an alternative to reliance on a BMT-specific QOL instrument, the current study will include a cancer-specific QOL measure. These measures have been well-validated in the literature and will be reviewed next.

Cancer-specific QOL measures have been in existence since the early 1980s (Meyerson, 1983). Several of the more well-validated measures will be reviewed below. The Functional Living Index-Cancer (FLIC) was one of the first measures to be validated in a cancer population (Jabroppe, Clark, Mithelany, & Lewis, 1984). The measure is cancer-specific, theoretically-oriented, designed for patient administration, and is reliable and valid. Four principal areas of functional importance were defined: 1) social satisfaction, 2) affect/psychological state, 3) social interaction, and 4) somatic sensation.

Several measures have been developed since that time which provide a total score such as the Cancer Rehabilitation Evaluation System Short Form (CARES-SF) (Jorgensen, Qvale & Hestvik, 1991), and the Functional Assessment of Cancer Therapy (FACT) (Cella et al., 1993). These measures are both well-validated and reliable for use in a cancer population.

The CARES-SF provides a total score and scores on five main domains: 1) physical functioning, 2) psychological functioning, 3) social functioning, 4) social interaction, 5) medical interaction. Psychometric properties of the CARES-SF have been

demonstrated (Haley, Cella, & Horowitz, 1991). The CQOL-100 contains total of 100 questions, making it one of the more time-consuming measures to complete.

The FACT scale is one of the most rigorously validated measures available for use in a cancer population. In addition, the FACT scale contains only 26 questions, and can be completed by patients in approximately 5 minutes. Data were collected over a five year time period on 141 patients at a variety of health centers, with a variety of cancer types. Factor analysis created five subscales: 1) physical well-being, 2) social well-being, 3) emotional well-being, 4) functional well-being, and 5) relationship with doctor. Convergent validity was high between this measure and other cancer specific QOL measures (Cella, et. al. 1993). In addition, the FACT was sufficiently sensitive to detect differences in QOL based on stage of disease. Test-retest coefficients for a sample of 50 patients were high, ranging from .81 to .92 for the five domain scales.

Another cancer-specific QOL measure which has been well received is the European Organization for Research and Treatment of Cancer (EORTC) 10 item quality of life scale. The EORTC QLQ-C10 encompasses five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), and a global health and quality of life scale. The questionnaire takes approximately 10 minutes to complete and is designed to be filled out by patients. All scales demonstrated adequate reliability and validity, with the exception of the role functioning scale, which is a step-down of the functional scales.

In sum, all of the cancer-specific QOL measures described above are strong from a psychometric standpoint. They are all applicable to a wide range of cancer types, and have adequate validity and reliability. For the purposes of the current study it was necessary to choose one of these established measures. The EORTC was eliminated from consideration due to the fact that its role functioning scale is not well validated. This was a concern, since it has been suggested that role functioning is critical for regarding adequate QOL following BMT (Pellegrino, et al., 1993). The CAMO-3P was eliminated from consideration due to its length. It has been pointed out formerly as an important consideration to improve compliance when choosing a QOL measure (Harrison et al., 1993). The FACT emerged in the current study due to its strong psychometric properties, and its brevity and applicability to a BMT population. This measure has been validated for use in a BMT population (Judykewitz, 1994).

CHAPTER 1 SPECIFIC AIMS AND HYPOTHESES

The current study focused on patients at least 3 months post-BMT. The purpose of the study was to determine the utility of pre-transplant variables (psychosocial, demographic and medical) in predicting survival, physical functioning and quality of life (QOL) post transplantation. The independent variables chosen for study have been previously associated with survival or quality of life in either a BMT population or a cancer population.

In terms of survival rates, it was hypothesized that: (1) significant affective symptoms (depression and anxiety), (2) lower levels of functional support, (3) a history of inadequate compliance with medical regimens (pre-BMT), (4) increased age at BMT, (5) increased time from initial diagnosis to BMT, (6) prior metastatic/recurrent/inoperable disease, (7) lower disease state (post initial treatment) and (8) allogeneic transplantation (as opposed to autologous BMT) would be associated with decreased survival rates. As noted above, these variables were chosen for study due to their association with survival or quality of life in either a BMT or cancer population. The predictive utility of affective symptoms on survival and quality of life has been reviewed above. Higher levels of functional support have been associated with increased survival time and increased quality of life in a cancer population (Bl, et al. 1992; Cava, et al. 1991). Noncompliance and lower life-threatening symptoms (Gardelski, 1994) represent all of outcomes have

post-transplant behavior predicts mortality or morbidity in RMT. The demographic, disease, and treatment related variables were chosen for study because they have been associated with post-BMT mortality or morbidity in previous studies (Pan, Kharabi & McIntyre, 1991; Karmali & August, 1989).

In terms of quality of life, it was hypothesized that the above mentioned psychosocial, demographic and medical variables would be associated with poorer quality of life post-BMT. In terms of symptom self-report, it was hypothesized that the above mentioned psychosocial, demographic and medical variables would be associated with poorer quality of life postBMT.

In addition, several "secondary hypotheses" were investigated. In terms of psychosocial variables, it was hypothesized that (1) undergoing psychological or psychiatric treatment either during BMT or post-BMT and (2) experiencing significant life stressors post-BMT (e.g., death of a loved one, divorce, etc.) would be associated with increased mortality and morbidity post-BMT.

Several medical variables were examined. Within the diagnosis/BMT group, patients with chronic fatigue (Mazur, 1990 personal communication), it was suggested that diagnosis would be associated with life-threatening events, with acute leukemia patients and patients with myelodysplastic syndromes having increased mortality and morbidity compared to chronic myelogenous leukemia and splenic mass patients. Within the no-BMT group, it was hypothesized that patients with or without evidence of the

type of BMT would have increased mortality and morbidity compared to patients with no evidence of disease.

It was hypothesized that deceased subjects would have more symptoms of anxiety and depression pre-BMT, lower levels of social support and greater compliance. Finally, it was hypothesized that patients undergoing psychological treatment would experience improved quality of life and physical functioning post-BMT.

The results of this study add to the sparse existing literature investigating the impact of psychosocial variables on outcome as in a marrow transplantation. Investigation of the hypotheses above can assist in providing relevant information to the medical staff regarding who is likely to survive and adapt within BMT. The information should be used to determine which patients are appropriate for BMT and to identify interventions to aid patients at high risk for mortality or morbidity post-BMT. These interventions should be aimed at assisting high risk patients to become better recipients for BMT.

CHAPTER 4 METHODS

All protocols were reviewed and approved by the University of Florida Health Science Center's Institutional Review Board (IRB). No financial incentives were offered to the subjects for their participation in the study.

Demographics

One hundred and eight patients were contacted about participating in the study. Seventy-one subjects (54%) of those contacted were included in the analysis. Of these patients, 42% were male and 58% were female. The mean age of the patients at the time of BMT was 54 years. Patients had an average of 14 years of education. Mean length of time from diagnosis to time of transplant was 11 months (standard deviation = 14 months). Forty-three percent of the patients were in their first remission at the time of BMT. 14% were in a subsequent remission or relapse and 42% were relapsed for 14% of patients. Thirty-five percent of patients underwent allogeneic transplantation, with 65% undergoing autologous transplantation. At the time of post-BMT data collection, 55% of the study sample ($n=40$) were alive and 35% ($n=25$) were deceased. Patients completed post-BMT measures 2 months to six years after receiving their transplant. Mean survival time post-BMT was 34.3 months (sd=17.58 months). Forty-two patients refused to participate. Of these patients, two refused telephone interviews, five were not eligible to

received by telephone and did not receive telephone messages, and because all the patients did not return needed questionnaires. (See Table 1).

Table 1. Demographics, Disease, and Method Drop.

Variable	Percentage or value	SD and Range (if applicable)
Male	42%	
Female	58%	
Degrees		
M.D. or equivalent	14%	
Ph.D. or equivalent master's or other degrees	14%	
Other degrees	92%	
Research status		
First respondent	47%	
Second respondent or relative knowing data	52%	
Missing data	1%	
Trial/Study Type		
Adaptive	14%	
Analogous	86%	
Site status		
Active at follow-up	70%	
Discontinued at follow-up	30%	
Mean age at [Site]	33.4 years	(sd=12.76, range=3-68)
Mean years of education	13.7 years	(sd=3.5, range=9-20)
Mean months from diagnosis to [Site]	15.8 months	(sd=12.05, range=0-70)

Subjects

Eligibility criteria for participation in this study were as follows. (1) Subjects had completed a pre-BMT assessment in the Psychology Clinic at Shrews Hospital. University officials, during the period 1990-1992. (2) Subjects had subsequently undergone allogeneic or autologous/relapse marrow transplantations, (3) Subjects were at least 14 years old at time of transplantation and (4) Subjects were currently at least 3 months post BMT. During this time-period 1990-1992, approximately 140 bone marrow transplantations were performed in adult patients at Shrews Hospital. Subjects were recruited from this patient population.

Measures

As per the eligibility criteria, all patients were made for a pre-transplant psychological assessment in the Psychology Clinic at Shrews Hospital. Transplant-transplant assessment typically lasts 2-3 hours and consists of a clinical interview and psychological testing.

All psychological testing data were collected with interview data to form a composite the Transplant Candidate Evaluation Rating Form (TCERF) which contained assessment data relevant to transplantation. Similar instruments have been described in the literature as a way of assessing transplant candidates in terms of pre-transplant psychological variables (Dietrich & Lennert, 1989; Twiltman et al., 1992). The format of the TCERF is given under the data measuring

In the current study, the TCORF was read by two advanced graduate students who received training to ensure their understanding of the rating scale. One student served as the primary rater and the other served as a reliability rater. Prior to beginning the ratings of study subjects, rater practices completing the TCORF across "twelve" subjects independently. Intrinsic reliability was then measured to ensure the training was adequate. As recommended by Hartmann (1982), lower limits of acceptable percentage agreement ranged from 46-75. During the study, every fifth subject was evaluated by both raters as a check of inter-rater reliability.

Initially, data collection was planned to occur by telephone interviews. All potential subjects were mailed by mail that they would be contacted by phone regarding a research study. A brief description of the study was given in the letter and elaborated on via following phone call. This phone call served to inform the patients about the purpose of the study, answer any questions they had, inform them of any possible risks and benefits of participating, and obtain their consent to be involved in the study. Patients giving their consent were called in all but number of measures over the phone (see Measures section below). These measures consisted of a symptom checklist, a parent QOL instrument, and a caregiver/patient QOL instrument. The assessment lasted approximately one half-hour. Due to difficulties contacting patients by telephone, the correspondence of the above questionnaire was sent to most subjects (n=54) and they were provided with stamped envelopes in which to return the completed questionnaires. This correspondence is also

infectious methods is a potential confounding variable. However, two of the measures used, the FACT and the BAI-30, were designed to be administered either in a structured interview or by patient self-report and have demonstrated reliability in both settings (Johns/Kopke & Prill, 1992; Ware & Sherbourne, 1993).

Measures

Independent Variables

The operational properties of prospective BMT conditions are discussed directly in the time-of-pro-BMT assessment. However, the history of psychological tests administered varies considerably across patients because until recently there has been no specific assessment battery guidelines at this location. Specific tests administered typically (but not always) include subsets of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1971), the Minnesota Multiphasic Personality Inventory (MMPI) (Mallinckrodt & McCusker, 1976), the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970), and the Beck Depression Inventory (BDI) (Beck et al., 1988).

The MMPI is often used to assess personality functioning at four various implementation conditions. The MMPI is an originally derived measure and contains 48 clinical scales, four validity scales, and four supplementary scales. The MMPI has been administered in many populations and has adequate reliability and validity. For a detailed description of the MMPI, see Tellegen & Wittink and Tellegen (1972).

Negative affect is typically measured by the STAI and the BDI. The STAI is a 40-item questionnaire which measures two aspects of anxiety: state anxiety and trait anxiety (Spielberger, Gorsuch & Lushene, 1970). State anxiety is anxiety which is caused by a current response to certain, specific conditions. Trait anxiety is defined as anxiety which is characteristic to nature and is not strongly specific. Reliability and validity have been established (Tanner et al., 1988; Spielberger & Vagg, 1984) and the STAI has been used extensively in a wide variety of populations (Mory, Nelson, Gershon, & Lerman, 1988; Jorres, Bann, & Klein, 1990; Gershon, Lushene, Smith, & Nelson, 1984).

The BDI is a 21-item questionnaire that measures depressive symptomatology such as insomnia, weight loss, feelings of isolation, pessimism, guilt, self-stigmatisation, etc. The measure provides a severity score, which can develop in depressive symptoms, and has been an index of depression. Reliability and validity of the measure have been extensively reviewed and are adequate (Beck, Berman, & Garber, 1988).

While these items are typically administered as part of the pre-RCT screening, there is sometimes a lot concern of variability and these tests are sometimes not used. The variability in psychological testing may be serious a problem. However, this was compensated for by conducting psychological test results and interview data as a component of psychological functioning using the Transplant Candidate Evaluation Rating Form (TCERF). The TCERF rates psychological functioning as a variety of domains including affect, coping/relaxation and social support. Each domain is rated on a five-point

Libert-type scale. Rates were split by a guideline which provided detailed descriptions of values for each severity rating. The descriptions are described below. As noted earlier, narrative reliability data was gathered to ensure the reliability of the measure. Also, in clinical practice there is no standard history of tests used to assess pre-BMT patients. Besides using scales on the TDEAF are just beginning to be described in the literature (Gilliland, Lewman, Hill, Twilings, et al., 1996). Therefore, this study is in line with current clinical practice and hopefully will serve to demonstrate a valid way in which clinical interview data can be combined with valid psychological testing data.

Three variables from the TDEAF were analyzed as potential independent variables: affect, social support and compliance history. Also measured as secondary variables were psychological or psychiatric treatment and life satisfaction. Patients were asked about past history of psychological treatment, as well as current opinions regarding the occurrence of physical life events since BMT.

As noted above, TDEAF variables were rated on a five-point scale. Rates were broken to use the scale using an expanded-description form. On the affect domain a score of one on the affect scale is described as follows: "At least two of the following criteria met: (1) concerns about anxiety or depression or other emotion measured on psychological evaluation which is severe enough to cause concern about the recipient's suitability for transplant, (2) history of one or more psychiatric hospital admissions or admissions that are in attempt to manage psychological evaluation." A score of two is described as

follows: "Psychological evaluation questions appropriate about anxiety, anger, and sadness. Anxiety and depression are within normal limits." Similarly detailed descriptions of the ratings are listed for all members of ratings on all these scales. For the social support variable, a score of one represents the following: "Both of the following statements are a positive impact that this does not have value will be the primary caregiver following BMT and/or patient reports on strong relationships or very positive relationships." A score of three represents the following: "Stable, connected relationships, good mental health in social support system consistent in terms with patient throughout BMT process." For the compliance variable, a score of one is described as follows: "Complies with all of the following are included in the psychological evaluation: a. difficulty being compliant with medications, b. frequent missed appointments with medical, psychological services or behaviors in experiments and/or problems with dietary, exercise and smoking demands." A score of five represents that the patient: "Has no recent compliance history." No concerns are noted in the psychological evaluation." For all variables, a score of zero indicates that the item is "unable to rate" for that domain.

Also included were disease, treatment, and demographic variables that have been shown to have either an empirical or theoretical connection with BMT mortality and morbidity. These variables included: age at BMT, transfusion dependent to BMT status of various graft match (heterozygous to haploidentical or mismatch unrelated donor (MUD)), type of transplant (autologous vs. allogeneic) and disease stage (for patients in

Best disease phase vs. all other best stages). Secondary demographic and medical variables measured were socioeconomic status (SES) and, as proxy for that, the education level (high school and nonhigh school) and insurance status (in the employer-provided HMO group).

Outcome Variables

Three variables were measured post-transplant: survival, quality of life (QOL), and physical functioning/functional symptoms. Two methods were used to determine survival: death certificate. First, survival data were kept on record at Glens Hospital and if the patient was deceased, the death date was noted. If the patients survival status is unknown, this was obtained via telephone interview with the proxy, or the spouse or significant other if the proxy was deceased. If the patient was deceased, the date of death was obtained from the spouse or significant other.

Two Health Related Quality of Life (HRQOL) measures were used. First, the Medical Outcomes Study 36 Item Short Form (SF-36), a generic HRQOL measure, was administered. The measure was both internally and externally developed by Ware and colleagues (Ware & Sherbourne, 1993; McHorney, Ware, Rognes, Kosinski, & Le, 1993; McHorney, Ware, Le, & Sherbourne, 1994). The SF-36 contains eight health concepts including: limitations in physical activities because of health problems; limitations in social activities because of physical or emotional problems; limitations in role activities because of health problems; limitations in role activities due to emotional problems; pain, general mental health (psychological status and well-being); vitality (energy and fatigue), and

patient perception of general health status. The survey is designed to be a self-report measure, or to be administered over the telephone by an interviewer. The sample of 1,000 adults, the internal reliability of the subscale ranged from .77 to .90 (Brennan et al., 1992).

Also, a cancer-specific HRQOL measure was given. The literature is generally inconsistent on QOL measures specifically naming QOL in a breast cancer transplantee population. Therefore, a cancer-specific QOL instrument will be administered. The EORTC-QoL a cancer-specific instrument which includes overall-QOL items, as well as four subscale scores for physical, functional, social, and emotional well-being, and a subscale on satisfaction with treatment relationship items. The measure has demonstrated adequate internal consistency and reliability (Kahn, et al., 1990).

A symptom checklist was added to the post-transplantation battery in order to obtain information about post-transplant physical/medical condition. The Symptom Frequency Questionnaire, which has been modified after the work of Lough et al. (1987), was used for measurement. This questionnaire measures the frequency of 16 symptoms using a 5-4 rating (3 times/last symptom and 4 times/less symptom). In addition, for each symptom, the questionnaire requires, "Is this a problem for you?" The symptom frequency checklist yields two scores. The first is a "total frequency score" (sum of 5-4 ratings on all symptoms). The second is a "total problem score" (number of "yes"

responses on the questionnaire. These 2 items were analyzed as relevant physical functioning-related variables.

Finally, the Translating Research into Information Questionnaire provided a structured format for capturing about socioeconomic status (SES), prior psychiatric or psychological treatment, and significant life events/able stress in the past 6 months. Socioeconomic status was measured on a 5-point Likert-type scale, with prior psychiatric treatment and significant life events were analyzed as dichotomous variables (yes/no). Means and standard deviations for dependent and independent measures are presented in Table 1.

Statistical Analysis

Agreement reliability data were produced on the TCSRF by computing percentage agreement (Cohen, 1988).

Next, it was hypothesized that negative psychosocial influences (higher pre-BMT levels of anxiety and depression, lower levels of family/social support, history of substance compliance with medical regimens pre-BMT), negative demographic indicators (increased age at BMT, increased time from initial diagnosis to BMT) and negative medical indicators (prior marrow graft match, later disease state and diagnosis, transplantations) would be associated with decreased survival time. Correlation coefficients were computed to estimate the association of various psychosocial, demographic and medical variables to survival time. Those variables showing at least a slight trend toward association ($p < .20$) were subjected to a stepwise Cox proportional

Table 2. Means and standard deviations of measures.

Measure	Mean	SD
Telephone Careless-Deviation Rating Form (TCDRF)		
Social Support	4.14	89
Adher	4.14	91
Compliance	4.25	92
Life Stress	1.77	1.94
Functional Assessment of Cancer (FACT)		
Physical Well-Being	3.30	9.87
Emotional Well-Being	3.39	2.68
Social Functioning	3.09	1.96
Family Well-Being	3.49	9.87
Total Score	32.41	9.40
SP-36		
General Health Scale	49.21	20.28
General Mental Health	55.63	19.56
Symptom Checklist		
Problem Score	4.77	7.94
Frequency Score	27.04	16.26

Zero-inflated negative binomial model. The negative binomial model is a multivariate regression technique that estimates the relative contributions of each psychosocial, demographic, and medical variable to prediction of survival time post-BMT.

Second, it was hypothesized that those negative psychosocial indicators, demographic indicators and medical indicators would be associated with poorer quality of life post-BMT. Again, correlation coefficients were computed to assess the relationship between psychosocial, demographic and medical variables with quality of life. Variables showing at least a trend ($p < .20$) toward an association with QOL and symptoms self-report were included in a number of multiple linear regression models analyzing the utility of psychosocial variables in predicting post-BMT quality of life.

Specifically, multiple regression equations were analyzed for two domains of the SF-36: 1) general mental health and 2) patient perception of general health status. These domains were chosen because of their adequate internal reliability and because they address the most general and relevant variables of interest in this study. The predicted total of 11 multiple regression equations measuring the contribution of relevant demographic, psychosocial, and medical variables to the prediction of general mental health and patient perception of general health status.

For the FACT-G analysis, one multiple regression equation was used to measure the association of various demographic, medical, and psychosocial variables with the total score on the FACT-G. Also, ten multiple regression equations were used to measure the association of the independent variables with each of the domain scores: 1) physical well-being, 2) functional well-being, 3) social well-being, 4) emotional well-being, and 5) healthcare well-being and satisfaction.

Third, it was hypothesized that negative psychological, demographic and medical variables would be associated with increased symptom self-report. Again, correlation coefficients were computed measuring the association of psychological, demographic and medical variables with symptom self-report. Variables demonstrating a linear slight trend toward a significant association ($p < .10$) were included in multiple regression equations. A total of ten multiple regressions were performed to examine the symptom checklist variables. These multiple regressions measured the association of different demographic, psychological, and medical variables to: 1) the total frequency score, and 2) the total problem score.

Several secondary hypotheses were also investigated. First, it was hypothesized that patients undergoing psychological or psychiatric treatment either during BMT or post-BMT would experience decreased mortality and morbidity post-BMT. A t-test was run to examine this hypothesis. Second, it was hypothesized that patients experiencing significant life stress post-BMT would experience increased mortality and morbidity post-BMT. This was examined by computing correlation coefficients measuring the association of life stress with outcomes, quality of life and symptom self-report. Life stress was found to be at least slightly correlated to mortality or morbidity ($p < .10$) would be included in best regression analysis or multiple regression analysis as described above. Several hypotheses regarding the effect of medical variables on outcomes (see Chapter 7) had to be dropped from the analysis due to lack of data.

T-tests were performed to investigate whether disadvantaged and well-being subjects differed in terms of their pre-life/T effect, social support and compliance. T-tests were also run comparing subjects having psychological treatment in terms of their outcome (quality of life, survival time, physical functioning).

CHAPTER 3 RESULTS

Interrater Reliability

Interrater reliability was calculated as described above. Every fifth subject (50% of the order sample) was evaluated by both raters in cross-check coding. This yielded a sample of 11 subjects for whom percentage agreement was computed. Percentage agreement was 80.0% for Initial Support, 71.0% for Adher and 80.0% for Compliance. These values are within the guidelines suggested by Hartmann (1982) for acceptable interrater reliability in the social sciences.

Variables Included/Excluded from Multiple Regressions and Bivariate Analyses

As noted in the Statistical Analysis Plan, correlation coefficients were computed to investigate the association between pre-BMT demographic, physical/medical and psychosocial variables (independent variables) and post-BMT survival time, quality of life and physical functioning (dependent variables). Independent variables showing a least a slight relationship to variables with outcome variables were included in either Cox regression analysis or multiple regression analysis.

Survival time. The following variables showed a weak to moderate association with survival time and were therefore included in the Cox regression analysis: age ($r = .14$, $p = .02$) and BCR ($r = .02$, $p = .88$) (demographic variables); treatment type ($r = .31$, $p = .04$), treatment status ($r = .33$, $p = .04$), diagnosis (in allogeneic transplant) ($r = .05$, $p = .78$) and

number of medications ($p = .15$, $p = .17$) (medical variables). Affect, social support, and compliance/therapy were also included in the Cox regression analyses since they were the primary psychological variables of interest. Variables demonstrating no relationship ($p > .10$) to survival from multiple therapy use included in the Cox analyses are as follows: education, age at BHFT, gender and time from diagnosis to BHFT. Quality of outcome, graft result was dropped from the analyses because the low number of subjects for whom this information could be provided from medical records.

QOL and Symptom Self-Report: The following variables showed a trend toward an association with quality of life variables or symptom report variables and were therefore included in a number of multiple regression equations: age at BHFT ($p = .21$ NS, $p = .04$, education ($p = .28$, $p = .17$), BHFT ($p = .28$, $p = .02$) (demographic variables), and pain/BHFT effect ($p = .34$, $p < .001$), social support ($p = .27$, $p = .07$), compliance ($p = .28$, $p = .03$) and life stress ($p = .13$, $p = .003$) (psychosocial variables). The following variables did not show an association to quality of life or symptom report ($p > .10$) and therefore were eliminated from multiple regression analyses: gender, psychological or psychiatric treatment history (diagnosis, treatment type), treatment status (up/st, study as intended), chronic status and time from diagnosis to BHFT. Quality of graft result was eliminated as a variable due to insufficient sample size for which this information could be provided.

Survival Analysis and Multiple Regression

In terms of survival time analysis, none of the medical, demographic, or psychological variables significantly predicted post-BMT survival time. Given the robustness of the literature, it is likely that no set of predictors does have significant predictive value (Ardelt/Beckwith et al., 1994); however, this variable was dropped from the analysis due to its difficulty preserving the information from medical records.

In terms of the multiple regression analyses performed on the SF-36-General Medical and Psychological Scales, none of the medical, demographic, or psychological variables was predictive of responses on the SF-36-General Mental Health Scale, although pre-BMT affect showed a trend toward significance ($\beta=1.6$, $p=.06$). Patients experiencing higher levels of affective distress (pre-BMT) were more likely to rate their mental health as poor following treatment.

None of the medical variables was predictive of patients' responses on the SF-36-General Health Scale. However, patients experiencing lower life stresses were more likely to rate their post-BMT health as a positive status ($\beta=3.3$, $p<.05$). Also, patients experiencing lower levels of negative affect (pre-BMT affect) were more likely to rate their post-BMT health highly ($\beta=3.22$, $p<.05$). Interestingly, patients who reported lower levels of social support (pre-BMT) were more likely to rate their health as a positive status (post-BMT) ($\beta=3.7$, $p<.05$). Also, patients who ranked poorly in terms of pre-BMT coping/awareness were more likely to rate their general health as good post-BMT ($\beta=3.4$, $p<.05$).

None of the medical, demographic, or psychosocial variables was significantly correlated to subjects' Functional Assessment of Cancer (FACT-G) Total score, the FACT-G Family Well-Being Scale or the Functional Well-Being Scale. However, pre-BMT effect was predictor of post-BMT scores on the FACT-G Physical Well-Being Scale ($\beta=0.35$, $p<0.05$). Pre-BMT social support ($\beta=0.44$, $p<0.05$) and compliance ($\beta=0.41$, $p<0.05$) also significantly predicted physical well-being. In some subjects judged to have lower levels of negative affect, pre-BMT affect, higher levels of social support and better compliance history were more likely to report feeling physically healthy on the FACT-G Physical Well-Being Scale.

Several medical, demographic and psychosocial variables were associated with decreased scores on the FACT-G Satisfaction with Doctor scale. The following variables were significantly correlated with decreased satisfaction with the treating physician: male gender ($\beta=-.33$, $p<0.05$), lower SES ($\beta=-.40$, $p<0.05$), diagnosis: leukemia ($\beta=-1.1$, $p<0.05$), decreased life stress ($\beta=-1.4$, $p<0.05$), decreased negative affect pre-BMT ($\beta=1.4$, $p<0.05$), lower levels of pre-BMT social support ($\beta=1.4$, $p<0.05$) and poorer pre-BMT compliance ($\beta=1.4$, $p<0.05$).

No medical or demographic variables were significantly correlated with Frequency of Symptoms (see Symptom Checklist). However, patients experiencing more life stress experienced greater frequency of symptoms ($\beta=1.1$, $p<0.05$), and patients with more symptoms of anxiety and depression pre-BMT ($\beta=0.8$, $p<0.05$) and poorer compliance

($F=3.7, p<.05$). Patients judged to have higher levels of social support pre-BMT significantly reported greater frequency of symptoms post-BMT ($F=3.4, p<.05$).

In terms of how disturbing subjects reported their physical symptoms to be (Symptom Checklist Total Problem Score), subjects with higher levels of negative affect pre-BMT ($F=3.3, p<.05$) and poorer compliance ($F=3.4, p<.05$) judged their symptoms to be more problematic than did subjects with higher ratings of pre-BMT affect and compliance. Also, subjects with higher levels of pre-BMT social support rated their symptoms as more disturbing than did individuals with lower levels of social support ($F=2.4, p<.05$).

Follow-up

T-tests were run comparing deceased individuals with individuals still living at time of their pre-BMT affect, compliance and social support. Individuals with lower levels of social support pre-BMT were more likely to be deceased at time of follow-up (one-tailed $t=1.72, p<.05$). Individuals with higher levels of negative affect pre-BMT showed a trend toward being more likely to report during the follow-up period compared with individuals with lower levels of negative affect pre-BMT (one-tailed $t=1.48, p=.06$).

T-tests were also performed comparing individuals who had received psychological or psychiatric treatment with those who had not in terms of their survival rates, likelihood of being alive at time of follow-up, quality of physical symptoms report. The only significant result was for individuals who had received psychological treatment

reported greater frequency of symptoms (Z -value 1.143, $p < .01$) and greater distress about these symptoms (Z -value 1.136, $p < .01$) than individuals who had not received psychological treatment (see Tables 3 and 4).

Table 2 Results of regression analyses on predictors of quality of life and symptom report

Outcome variable	Significant predictors	Beta	Adjusted R ²	F
SF-36 General Health			.70	3.04
	Lubricant	-.07		
	Adhes	-.09		
	Social Support	-.03		
	Compliance	-.04		
FACT Physical Well-Being			.55	3.43
	Adhes	-.08		
	Social Support	-.01		
	Compliance	-.03		
FACT Symptom subscale (all)			.60	3.00
	Gender	.10		
	SES	-.02		
	Transplant type	.04		
	Lubricant	-.02		
	Adhes	.01		
	Social Support	-.12		
	Compliance	-.11		
Symptom Checklist-Frequency			.77	3.76
	Lubricant	.44		
	Adhes	-.25		
	Social Support	.03		
	Compliance	-.02		
Symptom Checklist-Problems			.53	3.38
	Adhes	-.41		
	Social Support	.11		
	Compliance	-.09		

Table 1 Psychological Variables significantly associated with mortality (QOL and symptom impact)

Variable	Association
Social support	1. Subjects with poor pre-BMT social support more likely to be deceased at follow-up 2. Adequate pre-BMT social support predicts decreased differential anxiety level, increased symptom frequency and symptom distress at follow-up
Effect	1. Subjects with fewer symptoms of depression and anxiety pre-BMT have more positive perceptions of their health, decreased symptom frequency and symptom distress at follow-up
Compliance	1. Increased pre-BMT compliance predicts decreased symptom distress and symptom distress
Lifestyle	1. Increased life stress predicts poorer perceptions of general health, increased symptom frequency and symptom distress

CHAPTER 4 DISCUSSION

Our psychological, demographic and medical variables were predictors of survival time. This is likely in itself, known in other studies (e.g., Antikarov *et al.*, 1994), quality of nursing-patient match was significantly predictive of survival time. In the current study, however, difficulty obtaining medical record data limited the inclusion of this variable from analysis. Based on the literature (Jeffrey, Jenkins & Whistler, 1994; Antikarov *et al.*, 1994; Jenkins *et al.*, 1994), it does appear that survival time is mediated predominantly by medical variables rather than psychological or demographic variables. Jenkins *et al.* (1994) notes that psychological variables appear to have a more pronounced effect on quality of life and pain. Wall examined more than mortality. Murphy, Jenkins & Whistler (1994) failed to find a significant link between depression and survival. Gregorich *et al.* (1995) found that sustained level of anxiety during the first week of ICU was significantly predictive of developing acute OHSU (Stage II-P) but was not predictive of eventual mortality. This suggests that psychological factors may play a role in medical morbidity but may have less subtle an effect to actually influence mortality. These studies were consistent to the only study to date which has linked psychological factors (depression and low family support) to mortality (Calvin, *et al.*, 1991). It should be noted that there are methodologic problems with the Calvin *et al.* study and the reader here can best appreciate

In the current study, subjects who were judged to have lower levels of social support were more likely to be depressed at time of follow-up compared to subjects with adequate social support. Although there is a great deal of literature linking social support to emotional adjustment (e.g., cancer) (see Rowland, 1984 for a review), few studies have investigated the relationship between naturally occurring social support (i.e., families, friends in the community) and mortality. To date, only Cohen et al. (1983) has measured naturally occurring social support separately and their outcomes on cardiovascular or mortality. Cohen et al. (1983) found that individuals undergoing BMT who reported adequate family support were more likely to be alive at the time of follow-up compared to individuals who rated their family support as poor. Longenecker et al. (1986) has suggested that psychosocial factors (such as social networks and social support) may influence effectiveness through the issue of cognition, which plays a role in connecting the neuroendocrine and immune systems.

Research has also investigated the effect of social support interventions on mortality. According to Holland (1983) over 20 intervention studies have been conducted that tested social interventions. The majority of which demonstrated an improvement in psychological adjustment. However, the data on mortality are more equivocal. Most of the social support intervention studies looked at social interventions and behavioral/psychological focus. These studies focused on either post diagnosis or pre diagnosis (see Holgans & Cohen, 1984 for a review of this research). Holgans & Cohen conclude that

although their review includes several studies that found effects of social support interventions on mortality (Tewey et al., 1991; Montgomery et al., 1994; Sjogard et al., 1995), the number of studies focusing on mortality as a primary endpoint was not sufficient to assess the effectiveness of these interventions or to speculate on hypothesized mechanisms for the protective effect of social support. In sum, it appears that social support may protect people to some extent from mortality. However, the most helpful type of social support (i.e., family support vs. peer discussion group vs. peer education group) has not yet been determined. The "protective" components of a peer discussion group may be very different from the "protective" components in a naturally occurring social support group (like a family). Further research needs to clarify exactly what components of naturally occurring social support and social support interventions protect people from mortality and morbidity. This would enable identification of individuals at increased risk of mortality to gain increased social support and would allow interventions designed to address the specific components of social support which protect individuals from mortality.

People who reported elevated levels of life stressors, e.g., divorce, death of a loved one, illness, loss of job at the time of follow-up reported poorer perceptions of their general health and more frequent symptoms of illness than did individuals who reported low or no life stressors. This again points to a connection between an individual's psychological state and his or her perceptions of physical health. Stressors tend to interfere with

competence versus quest and IPA subs, thereby increasing positive functioning. (Meyer-Wiskow & Flehner, 1994; Ross, Katter & Isenhardt, 1995). Consistent with this, it was also found that recipients who had lower levels of negative affect pre-BMT had more positive perceptions of their general health at the time of follow-up. Further, individuals with lower levels of negative affect pre-BMT reported decreased symptoms/frequency and were less distressed by the symptoms which they did experience. This is consistent with Gregorich et al. (1996) who found that subjects undergoing BMT who had elevated anxiety levels were most likely to develop acute GVHD.

Recent trials suggested (Raker et al., 1994; McMill & Wallisch, 1996) as well as Raker et al. (1995) that self-esteem may play a large role in determining adaptive functioning and perception of physical health following BMT. Individuals with improved self-esteem scores 4 days before post-BMT than individuals with low self-esteem. While self-esteem was not measured in the current study, it would be expected that self-esteem would play a large role in determining post-BMT distress score. Since having adequate self-esteem may enable people to experience improved affect, having pre- and post-BMT this is an area needing further research. Learning how certain people maintain their self-esteem and improve post-BMT quality of life as the time of rising physical, medical status and emotional changes would better the development of interventions designed to aid those with poor self-esteem both pre-BMT and during BMT.

Conflicting data were found with regard to the impact of social support and compliance on perceptions of physical health. On the SF-36, patients who had lower levels of social support and compliance rated their physical health as better than individuals with higher levels of social support and compliance. However, on the FACT-G, patients were more likely to report good physical health who had higher levels of social support and compliance pre-RMT. This may be due to the fact that the SF-36 and the FACT-G measure widely differing things. The SF-36 is a general health survey, while the FACT-G is a cancer-specific quality-of-life instrument. As a result, the SF-36 focuses on general activity level as a way of measuring physical health, while the FACT-G focuses on cancer-specific physical symptoms as a measure of physical health. Looked at in this light, individuals with lower levels of social support may be forced to be more active and independent than those subjects with social support networks to help them complete activities. Therefore, based on reports of physical activity, individuals with low social support would appear to rate themselves as healthier than individuals with more social support. At any rate, the relationship between social support, compliance and perceptions of physical health remains unresolved at this time.

With regard to symptoms/frequency and distress related to symptoms, individuals with higher levels of pre-RMT social support and greater compliance reported higher levels of symptoms and more emotional distress over those symptoms. It would be expected that individuals with poorer compliance behaviors would experience more

symptoms. However, the relationship between social support and symptoms requires further study. It is possible that caregivers tend to focus on symptoms as an attempt to make men of prostate feeling the pressure to “accept” symptoms seem less like an overall ill-finding. However, independently of family and friends.

However, it is also possible that individuals’ level of social support changed from pre- to post-BMT. Little research has focused on what changes take place in terms of family relationships during and following BMT. One study (Lippman, et al., 1994) found that there was little change in social support over time, however, another study (Zabner, et al., 1992) found that there were great changes in social support over time with some patients reporting increased social support and others reporting decreased support. This means that level of social support prior to BMT may not mean post-BMT level of social support post-BMT. This in turn would make it difficult to predict quality of life post-BMT based on pre-BMT social support. Zabner and colleagues found that families reacted in all sorts of ways to periods in which they reported the BMT patient as more lonely and more roles, and when these goals were not fulfilled, family conflict was higher. They also found that, in general, BMT patients’ significant others experienced a significant worsening in their emotional state up to six months after BMT as well as reporting decreased physical fatigue. In sum, the fact that little research shows changes in social support over time for BMT patients makes it difficult to make inferences about the

relationship of pre-BMT social support to post-BMT report of physical symptoms in BMT patients.

Social support was not found to correlate with post-BMT effective coping. Individuals with lower levels of social support were not more likely to report emotional distress or follow up. This is in contrast to Baker et al. (1994) who found that patients with low social support were more likely to experience high levels of anger and negative affect post-transplant. However, in the Baker et al. study, patients were reporting social support pre-BMT. Therefore, these patients may be expected to experience anger and negative affect in response to the current state of low family support. As noted above, it is unclear in the present data how or if social support changes during the time between pre-transplant and one-year post-transplant (Berglund, 1994). Patients in our study were initially social support pre-BMT and those with low levels of support pre-BMT may have improved their level of social support during and after transplantation. Indeed, at least one study has found that social adjustment post-BMT is comparable with a healthy community sample overall in various domains of work, family, marital and leisure activities (Chakrav, Wallack & Ferry, 1986), suggesting that BMT patients assimilate well into their communities following BMT.

Individuals in the current study who had undergone psychological or psychiatric treatment in the past were more likely to rate their frequency of physical symptoms as high. This is likely due to the fact that individuals with more severe physical symptoms

may be more emotionally distressed than individuals with few symptoms and therefore, more likely to require psychiatric treatment. Individuals on the Stress Management Unit at the University of Florida are monitored closely by the staff, who notify the Psychology Dept. if psychological distress appears to be in excess of normal levels. At that time, psychotherapy is typically initiated.

A relatively low rate of nonresponse to the FACT 9-dimensional scale factor scale. In the current study, indeed, people with lower symptoms levels (anxiety, depression, social support and compliance), people with fewer symptoms of anxiety and/or depression pre-BMT, and people undergoing allogeneic treatment were more likely to have higher ratings of satisfaction with their doctor. This suggests that patients who have lower levels of social support may look for this support in their treating physician. Also, patients with lower BCL and fewer distress symptoms pre-BMT may be more likely to trust their physician and therefore, report increased satisfaction. Individuals receiving allogeneic treatment may report higher patient satisfaction due to having increased contact with their doctors compared to autologous BMT patients. This would likely be due to the fact that allogeneic BMT involves a more likely to experience GVHD necessitating closer follow-up after BMT and increased contact with medical staff. It is unclear why individuals with greater pre-BMT compliance would have higher physician satisfaction.

In summary, pre-BMT psychological variables appear linked to outcomes in terms of both secondary and psychological morbidity. People with higher levels of anxiety and/or

diagnosed pre-transplant were more likely to report poorer perception of physical health, greater frequency of symptoms and greater distress about these symptoms. Despite this, lower levels of social support appear to be a stronger risk for mortality compared to those with higher levels of social support. However, higher levels of social support may cause individuals to focus on their symptoms more than they otherwise would and so decrease their activity level overall. Individuals with higher levels of social support reported more frequent symptoms and more distress about these symptoms than did individuals with lower levels of social support.

The current findings are very encouraging, as they suggest that psychosocial factors do have a strong influence on outcomes in terms of quality of life and possibly mortality. This is important because interventions designed to modify patients' affective state, level of social support and compliance behavior are common in the literature, but only now are beginning to receive strong empirical support (e.g., Andrykowski et al., 1994; Granger et al., 1994). The clinical implications for the current study are important. First, the role of psychology in assessing patients for risk factors as well as in strengthening prior to the current trial. Also, treating physicians should know that outcomes may be improved if a patient's affective state is closely monitored and interventions put in place at the first sign of affective distress in terms of social

There are several limitations of the current study. The first is the retrospective nature of the design. The second is the use of a subjective rating scale to measure

subjective pre-transition psychological functioning. However, the subjectivity rating scales are modified after several other rating scales found to have adequate reliability and validity in a BMT population (Forsberg, et al., 1994). Thus, the sample size was somewhat small limiting statistical power. Definitely a decreasing method information was another limiting factor/manifesting the limitations of several important method problems associated from the analysis. Future studies should use a prospective design and standardized psychological measures (e.g., de Jongh et al., 1999 and Andrykowski et al., 1994 studies).

Related to the limitations above is the response rate of the current study. Since only 64% of those contacted/eligible participants in the study actually participated, it is interesting to question whether a sufficiently large sample made its own or is significantly different from a true cross-section of EMT workers. While there is no research examining this issue in a EMT population, it is not expected that there would be any differences between study participants and non-participants. Additionally, participants in the study had a wide range of experience in terms of quality of life. Some were quite pleased with the results, reporting the side-effects and/or lingering symptoms, while other EMT patients reported adverse QWOL difficulty returning to work, and problems in physical and emotional functioning. It is therefore suggested that the compliance rate study is likely representative of EMT workers as a whole.

Future research should also address the complex relationship between social support and mortality. It remains possible that higher levels of social support protect patients from mortality (Folgerow & Cohen, 1994). It is not yet clear which types of social support (i.e., family support vs. peer discussion or educational support groups) are the most helpful in decreasing mortality. Moreover, it may be true that particular types of social support (for example, cancer support groups) which motivate patients to increase their independence and take on active roles in maintaining social support networks may be the most effective in decreasing psychological morbidity (i.e., quality of life symptoms report) as well as mortality. Based on the current study, interventions such as group or individual psychotherapy which (hopefully) increase patient independence, provide social support and decrease depression and anxiety could "modulate" people against mortality and morbidity post-BMT.

The complex role between social support, risk reduction, and quality of life should also be further studied. It appears that only survivors are useful compared to decreasing not only BMT patients' quality of life, but also thereby decreasing post-BMT (Baker, et al., 1997). The newer a BMT patient is able to receive take such as family members, parents, employees, etc. the better the family and unable to receive normal functioning. While medical variables certainly play the largest role in an individual's ability to receive typical role functioning, psychological variables also play a part. Since it is unclear what changes occur in social support over time following BMT, more research is

creative ways to allow BMF patients to most control over their treatment and life style following BMT, thereby increasing their ability to restore role functioning, increase social support and helpfully protect themselves from increased risk of anxiety and morbidity.

Finally, continued research into the development and refinement of rating scales similar to the one used in this study (see Appendix 1) will be helpful. Given the current state of clinical practice this involves the use of a multidisciplinary psychological assessment techniques and instruments, finding a means of automating timing and scoring data, a valid and reliable way associated to identifying patients at high risk for negative response to BMT. Particular issues to focus on include the measurement of reliability between samples of BMF patients and between raters.

REFERENCES

- Anderson, B. K., Alvestrand, A., Bergman, B., Bellingar, M., Dall, A., Deim, N. J., Tildesley, M. A. (1992). The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials oncology. *Journal of the National Cancer Institute*, **183**, 141-154.
- Anderson, B. K., Gargrak, B. D. & Pyle, M. A. (1991). Post-operative adjustment of bone marrow transplant survivors. *Bone Marrow Transplantation*, **7**, 111-114.
- Andersson, M. A. (1994a). Psychological factors in bone marrow transplantation: a review and recommendations for research. *Bone Marrow Transplantation*, **11**, 193-198.
- Andersson, M. A. (1994b). Psychiatric and psychosocial aspects of bone marrow transplantation. *Psychosomatica*, **11**, 13-14.
- Andersson, M. A., Alvestrand, A. M., Boman, K. L., Ekerdt, T. O., Gargrak, B. & Gustav-Denney, P. J. (1992). Cognitive dysfunction in adult survivors of allogeneic bone marrow transplantation: relationship to dose-related body reactions. *Bone Marrow Transplantation*, **1**, 161-170.
- Andersson, M. A., Alvestrand, A. M., Boman, K. L., Ekerdt, T. O., Gargrak, B. & Gustav-Denney, P. J. (1993). The quality of life in adult survivors of allogeneic bone marrow transplantation. *Transplantation*, **55**, 450-454.
- Andersson, M. A., Brady, M. J. & Gustav-Denney, P. J. (1994). Psychological and psychosocial functioning after allogeneic bone marrow transplantation for leukemia. *Psychosomatic Medicine*, **56**, 435-439.
- Andersson, M. A., Gustav-Denney, P. J. & Ford, M. G. (1991). Physical and psychological functioning of adult survivors of allogeneic bone marrow transplantation. *Bone Marrow Transplantation*, **6**, 13-41.
- Baker, A., Carlens, B. & Wingard, J. R. (1991). Bone reactions and quality of life of bone marrow-transplanted survivors. *Bone Marrow Transplantation*, **11**, 471-474.
- Baker, F., Wingard, J. R., Carlens, B., Lohm, J., Jelliffe, D., Murphy, L. & Lager, M. (1994). Quality of life of bone marrow transplantation long-term survivors. *Bone Marrow Transplantation*, **11**, 191-197.

Koraki, J., Rappaport, E., Tzioumis, J., Wilson, A. H., Kassis, J. L., & Pinedo, G. (1991). Male breast dysplasia following total autologous transplantation. *Breast/Mammary Transplantation*, 2(Suppl. 1), 14.

Kush, A. T., Stein, R. A., & Gidycz, M. G. (1988). Psychosocial properties of the Beck Depression Inventory: Twenty-five years of evidence. *Clinical Psychology Review*, 10, 77-108.

Kutler, D. C. (1989). Psychological factors in organ transplantation. *Clinical Psychology Review*, 1, 471-484.

Kutler, A. E. (1992). Quality of life: perceptions of long-term survivors of bone marrow transplantation. *Studies/Revue/Revue*, 15, 31-37.

Leopold, M., Kothua, S. A., Cough, W. B., & Glass, B. S. (1981). The volunteer impact profile: development and field testing of a health status measure. *Medical Care*, 19, 797-800.

Leiberg, E., West, P., & Ellis, J. (1984). A possible relationship between psychological factors and bone marrow. *Psychosomatic Medicine*, 46, 277-280.

Leiberg, E. K., Reid, W. R., Shaw, L. A., Hollier, J. C., Lofth, L. M., Makowski, D., Fisher, S. L., & Harris, T. B. (1989). Anticipatory immune suppression in women receiving cyclic chemotherapy for ovarian cancer. *Journal of Consulting and Clinical Psychology*, 57, 113-117.

Reese, H. H., & Kelly, M. J. (1991). Stages of bone marrow transplantation: a psychosocial perspective. *Psychosomatic Medicine*, 53, 438-448.

Colla, S. F., Tubley, D. S., & Gray, G. (1993). The increased awareness of cancer therapy risks: development and validation of the general cancer. *Journal of Clinical Oncology*, 11, 170-179.

Chang, R. E. (1988). Bone marrow transplantation: individual and societal issues. In R. Chang (Ed.), *Bone Marrow Transplantation* (pp. 1-17). Hobell: Mass: Stone Academic Publishers.

Chen, M. J., Turner, D. R., Wilson, J. R., Long, G. D., Mori, T. A., Goldstein, B. A., Wang, R. M., Hagan, A. S., Fleming, S. F., & Stone, R. G. (1992). *Psychosocial*

assessment of quality of life after radiotherapy for nasopharyngeal carcinoma. *Radiotherapy and Oncology*, 104, 42-48.

Christensen, A. F., Wells, J. E., Smith, T. W., & Turner, C. W. (1994). Predictors of survival among laryngeal cancer patients: effect of perceived family support. *Health Psychology*, 13(4), 501-509.

Cohen, J. (1988). A coefficient of agreement for nominal scales. *Educational and Psychological Measurement*, 28, 37-46.

Cohen, B. A., Cohen, A. L., Pappas, M. E., & McClure, P. B. (1991). Depressed mood and other variables related to late nasopharyngeal cancer in adult females. *Gynecologic Oncology*, 39, 426-429.

Cox, M. P., Wheatland, M. J., Fowles, R., Hunter, M., & Milliken, B. (1999). Chemoprevention and treatment of nasopharyngeal cancer after total body irradiation for leukemia. *British Medical Journal*, 319, 1494-1497.

Deffenbacher, W. G., Welsh, G. E., & Deffenbacher, L. B. (1975). *Anxiety* (Handbook (Vol. 1, 2)). Minneapolis: University of Minnesota Press.

Devos, G. M., Meert, J., Maréchal, P., Paul, L. C., Noss, A. B., Bergsma, E. D., Tack, K., Bolten, E., Lohmann, P. K., & Hooley, E. (1995). Psychosocial predictors of satisfaction and compliance in cancer. *The Journal of Cancer and Mental Diseases*, 17(3), 103-111.

Deussen, G. W., Lofgren, R., Smith, M. M., & Helzer, P. D. (1994). Cross-nationality of the State-Trait Anxiety Inventory with an alcoholic population. *Journal of Clinical Psychology*, 50(3), 425-433.

Ell, K., Nilsson, R., Melander, L., Mander, J., & Hansson, M. (1992). Social relations, social support, and survival among patients with cancer. *Journal of Psychosomatic Research*, 35, 331-341.

Fennell, P. J., Fennell, W. W., Hsiao, C. E., Shaloff, A., Gidycz, G., Foley, J. L., & Klerman, G. L. (1992). Malignant melanoma: Effects of an early structured psychiatric intervention, coping, and reflective state on recurrence and survival 7 years later. *Archives of General Psychiatry*, 49, 681-689.

Fennel, B., Grant, M., Schmidt, G. M., Mann, M., Whithead, C., Forstman, P., & Forman, S. J. (1992). The meaning of quality of life for bone marrow transplant recipients. *Cancer Nursing, 15*(3), 133-140.

Fennell, B. W. (1982). Current theory of psychological effects on cancer incidence and prognosis. *Journal of Psychooncological Research, 11*, 17-31.

Fennell, B. W., & Marshall, J. (1985). The role of stress, social support, and age in survival from breast cancer. *Journal of Psychooncological Research, 12*, 77-83.

Fukunaga, A. D., Balluck, D. E., Reed, G., & Cox, C. B. (1992). The psychosocial levels system: a new rating scale to identify and assess emotional difficulties during bone marrow transplantation. *Cancer Nursing, 15*, 173-181.

Goss, P. A., Lee, J. J., & Siu, J. (1992). Quality of life assessment: An independent prognostic variable for survival in lung cancer. *Cancer, 62*, 2131-2138.

Grossnik, B., Lohr, B., Hoyer, H., Bräuer, D., Lohke, I., Breyer, V., Henze, D., Wenzel, M., Jahn-Santenaro, J., & Klat, U. (1992). Anxiety is a possible predictor of acute GVHD. *Bone Marrow Transplantation, 13*, 545-550.

Grochowski, P. M., Schellhammer, M., Nathoff, A. J., Kay, M. G., Hafford, A. G., & Stewart, K. M. (1991). Behavioral conditioning, psychological distress, survival in 1991. *Cancer, Behavior, and Immunity, 1*, 149-155.

Harrison, D. P. (1992). *Assessing the dependability of observational data*. In D. P. Harrison (Ed.), *New Directions for Methodology of Social and Behavioral Science*. Long Beach: Center for Study Science.

Holmberg, S. R., & McKinley, J. C. (1979). *The Informatics Malady: Aids to Discovery, Learning*. Minneapolis, MN: National Computer Systems.

Holmes, V. B., & Cohen, S. (1986). Social support and adjustment to cancer: Reconciling descriptive, correlational, and intervention research. *Health Psychology, 15*(2), 129-141.

Hosgrain, M. W., Harrison, S. R., & Jones, F. E. (1991). Psychological aspects of bone marrow transplantation: a retrospective study of long-term survivors. *Bone Marrow Transplantation, 11*, 17-21.

Forbert, T. B., & Cohen, S. (1993). Depression and recovery: a meta-analytic review. *Psychological Bulletin*, 113(3), 473-494.

Folland, J. C. (1981). Psychological variables: Are they relevant to cancer risk or survival? In J. C. Folland, L. M. Laska, & M. F. Meenan (Eds.), *Cancer: Cognition in Health-Behavior* (2nd ed., 1984). New York: Memorial Sloan-Kettering Cancer Center.

Forrest, P. L., Lacey, M., Alexander, J., & Whitaker, J. (1994). A prospective study of psychological morbidity in adult bone marrow transplant recipients. *Psychosomatica*, 28(4), 344-362.

Forrest, H., & Aggar, C. S. (1984). Bone marrow transplantation: Problems and prospects. *Medical Clinics of North America*, 68, 407-434.

Kennedy, D. A., & Norwood, J. H. (1995). The clinical evaluation of chemotherapeutic agents in cancer. In C. MacLeod (Ed.), *Evaluation of Chemotherapeutic Agents* (p. 110). New York: Columbia University Press.

Kupper, D. L., Stolley, C., Brown, B., & Singer, M. (1981). Adjustment to renal transplantation. *Psychosomatica*, 24(7), 109-121.

Kendall, M. G. (1945). Rank and product-moment correlations. *Biometrika*, 36, 171-182.

Kramer, J. E., Cornsmaier, M. R., Bicker, P. E., Nier, W. M., & Corns, M. J. (1991). A prospective study of cognitive functioning following low-dose radiation for bone marrow transplantation. *Psychiatry*, 55, 447-462.

Koss, R. T., & Kossner, H. C. (1984). Effects of group therapy for patients with post-traumatic stress syndrome, body image, and sexuality. *Journal of Sex Research*, 22, 428-451.

Laporta, J. P., Brown, G., Lopez, M., Lohrke, M., Juan, J. P., Langa, S., Reichardt, J., Paulsen, L., Jones, P., & Neill-Winter, M. P. (1994). One hundred twenty-five adult patients with primary acute leukemia: categorized with marrow purged by multi-drug or 10 year single autologous response. *Blood*, 83(10), 3144-3158.

Laska, L. M., Goss, P. J. S., Mirman, G. H., Mastaglio, J. B., & Folland, J. C. (1992). Long-term psychological adjustment of acute leukemia survivors: impact of bone

coronary transplantation versus coronary搭桥术 therapy. *Psychosomatic Medicine*, **33**, 39-47.

Latham, R. W. & Connors, G. W. (1992). Depressed mood and development of cancer. *American Journal of Epidemiology*, **135**, 910-918.

Latessa, M. M., Rastegar, J. K. & Weiss, A. J. (1991). Quality of life: health aspects of heart disease transplantation. *Psychological Reports*, **75**, 195-198.

McClure, C. A., Ware, J. E., Rogers, W., Securi, A. E. & Lu, J. P. B. (1992). The validity and relative precision of HRQL short-and long-form health status scales and Demographic-COOP items. *Medical Care*, **30**, 982P-982P.

McClure, C. A., Ware, J. E., Lu, J. P. B. & Mosmann, C. D. (1994). The HRQL 14-item short-form health survey (SF-14): 83 Tests of data quality: coding, assumptions, and reliability across diverse patient groups. *Medical Care*, **32**, 40-52.

McKegan, L. W. & Finkel, G. S. (1991). Overview of health-related quality of life measures. *American Journal of Medical Pharmacology*, **43**, 1238-1243.

Moss, R. E., Wilson, J. K. & Pridgen, M. (1994). Psychosomatic oncology: the interface between behavior, brain, and immunity. *American Psychologist*, **49**(11), 1004-1017.

Murray, C. M. (1994). Measuring quality of life in emerging markets. *Statistics in Medicine*, **13**(2), 49-55.

Nice, V., Lathier, L. & Harris, J. W. (1991). The Karnofsky Performance Status Scale: an examination of interobserver reliability in community setting. *Cancer*, **71**, 2000-2004.

Nguyen, H., Geller, G. A., Walter, S. B., Gelfand, A. M. & Segal, B. E. (1994). The impact of a patient social support program on survival with breast cancer: The importance of statistical bias in program evaluation. *Journal of Clinical Oncology*, **12**, 913-921.

Norman, G. H., Winkler, D. & Lohr, L. M. (1992). Long-term psychosocial adjustment of acute leukemia survivors: impact of marrow transplantation versus conventional chemotherapy. *General Hospital Psychiatry*, **14**, 43-51.

Murphy, E. C., Jenkins, P. L. & Whitham, J. A. (1996). Psychosocial morbidity and survival in adult bone marrow transplant recipients: follow up study. *Scottish Medical Journal*, *41*, 555-562.

Muscar, J. (1991). Personality and survival time after bone marrow transplantation. *Journal of Psychosomatic Research*, *31*, 441-450.

Nagy, B. M., Palmer, D. V., Goodwin, J. & Rowson, B. G. (1992). Psychosocial compatibility of the donor: Translating Inventory for different ethnic subpopulations. *Psychological Assessment*, *5*(2), 343-349.

Olinick, M. E. & Levenson, J. L. (1978). Psychosocial adjustment of organ transplant candidates: Current status of neurobiological and physiological issues. *Psychosomatics*, *19*, 258-269.

Olinick, M. E., Levenson, J. L. & Flavin, B. (1977). The FACE: a rating scale for the study of clinical decision making in psychosocial screening of organ transplant candidates. *Clinical Transplantation*, *1*, 169-187.

Pan, M. D., Marcus, M. J. & Williams, W. (1991). Allergic bone marrow transplantation: Procedures and complications. *American Journal of Hospital Transplantation*, *1*, 179-189.

Parish, D. L. & Deyo, R. A. (1991). Gender and disease-specific outcomes in coronary heart disease and quality of life. *Clinical Cardiology*, *14*, 527-539.

Pauzella, W., Sauer, F., Grottel, L., Sauer, A., Freytagh, D., Pottel, J., Fogel, F., Burger, M. & Aglioni, M. (1997). Correlative angiography and self-control of human prostate hemostasis: new catheters from self blood. *Urology*, *49*, 1944-1953.

Pedberg, S. A. (1991). Rating scales for the psychosocial evaluation of organ transplant candidates: Comparison of the FACE and TRIM with bone marrow transplant patients. *Psychosomatics*, *32*, 438-441.

Pinto, J. M., Rao, R., Carreras, E., Jaffe, J., Sauer, J., Sauer, M., Kalle, M., Hsieh, T., Kuehler, R., Yama, R., Givens, R., Korman, C. & Davis, R. (1996). Physical and psychosocial features of 117 recipients of bone marrow transplantation. *Scottish Medical Journal*, *41*, 1133-1142.

Bowlus, J. H. (1987). Developmental stages and adaptation: A life model. In J. C. Norland, & J. H. Bowlus (Eds.), *Handbook of psychoanalytic psychotherapy: An offshoot of psychoanalysis* (pp. 15-46). New York: Oxford University Press.

Byers, J. J., Lunan, J., & Pedersen, A. (1993). Validity of the two critical subject short forms of the Wechsler Adult Intelligence Scale-Revised in a psychiatric sample. *Journal of Consulting and Clinical Psychology, 61*, 499.

Chang, C. A. C., Goss, P. A., & Stewart, R. L. (1991). Cancer Rehabilitation Evaluation System (Short Form-CESES-SF): A cancer-specific rehabilitation and quality of life instrument. *Cancer, 65*, 1406-1411.

Chapman, B., Clark, J., McWhorter, A., & Lewis, M. (1994). Measuring the quality of life of cancer patients: The Functional Living Index-Cancer: development and validation. *Journal of Clinical Oncology, 12*, 472-483.

Chenari, D. M., Miller, J. C., Fennell, R. J., Friedman, P. J., Degan, R. C., Goss, M. M., Finkel, D. B., Hest, T. A., Southam, A. A., Olin, N. J., & Skene, K. O. (1992). Extended follow up to 21 1/2 years: long-term allograft host marrow-transplant survivors: status of quality of life. *Transplantation, 53*, 351-357.

Chikala, R. B., Rapson, W. J., Gribble, A. M., Carver, D. C., Robinson, L. A., Lee, R. C., Wilson, C., & Ford, G. (1991). Psychological depression and 17-year risk of death from cancer. *Psychosomatic Medicine, 53*(1), 117-125.

Condon, A. C., Anglin, K., Benjamin, N., & Smith, P. (1990). Anxiety, stress and negative functioning in children who have undergone bone marrow transplantation. *Annals Paediatrics Scandinavia, 120*, 474-477.

Costa, O. R., & McDowell, B. M. (1993). Psychologically mediated effect on the delayed hypersensitivity reaction to tuberculin in humans. *Psychosomatic Medicine, 55*, 45-50.

Crump, D., Dixon, J. B., Krummel, H. C., & Goshal, B. (1985). Effect of psycho-social treatment on survival of patients with metastatic breast cancer. *Lancet, 2*, 1114-1114.

Derogatis, C. B., Gotsch, R. L., & Lofgren, R. B. (1978). *Stoa-Trait Anxiety Inventory Manual*. Palo Alto, CA: Consulting Psychologists Press.

- Spiegelberg, C. D., & Yagg, P. R. (1986). Psychometric properties of the SF-36: A reply to Rosenstock, Fennell, and Behl. *Journal of Personality Assessment*, 58(1), 89-97.
- Spitzer, W. D., Gibbon, M. J., & First, M. B. (1988). Measuring the quality of life of cancer patients: A concise QL-index for use by physicians. *Journal of Clinical Oncology*, 6(4), 582-591.
- Stein, M., Miller, A. H., & Treisman, A. L. (1991). Depression, the immune system, and health and illness. *Archives of General Psychiatry*, 48, 719-727.
- Stein, M., Kessler, R. C., & Sullivan, K. J. (1988). Stress and immunomodulation: the role of depression and neuroendocrine factors. *The Journal of Immunology*, 140(2), 627-633.
- Stewart, A. L., Derogatis, C. D., Fayer, R. D., Wells, K. B., Nelson, R. C., Klerman, G. L., et al. (1988). Summary and details of MOS instruments. In A. L. Stewart & J. B. Wells (Eds.), *Measuring functioning and well-being* (pp. 145-179). Durham, NC: Duke University Press.
- Stewart, P. R., Hays, R. D., & Alden, A. H. (1981). Psychometric properties of PTSD among PCW survivors. *Psychological Assessment*, 3(4), 104-112.
- Suzuki, K. I., Chapiro, M. R., Vignani, P. F., Cernigoi, C., & Sallera, E. M. (1991). Recovery after allogeneic marrow transplantation: a prospective study of predictors of long-term physical and psychological functioning. *Bone Marrow Transplantation*, 11, 119-127.
- Thomas, R. D. (1977). Bone cell transplantation: past, present and future. *Archives of Neurological Theory Experiments*, 35, 1-9.
- Tomlinson, J., & Brown, J. (1982). *Introduction to liver marrow transplantation*. In J. Tomlinson, J. Brown, & P. Ellis (Eds.), *Bone Marrow Transplantation in Practice* (pp. 1-6). New York: Churhill Livingstone.
- Tolson, S. M., McCann, B. B., Insel, D. C., & Mowbray, J. E. (1984). DSM-III classification of the anxiety disorders: A psychometric study. *Journal of Abnormal Psychology*, 93(2), 168-171.

Trullinger, R. E., Moore, C., Wolford, D. E., & Wickett, R. L. (1993). The Transplant Evaluation Survey/Scale: a revision of the Psychological Needs System for evaluating organ transplant candidates. *Transplantation*, *54*, 144-151.

Youn, J. M., Kennedy, B. C., Norman, P. J., Kinneging, A., & Armstrong, J. D. (1992). Long-term sequelae of xanthine base toxicity in peripheral stem-cell transplantation for lymphoid malignancies. *Cancer*, *65*, 784-791.

Wass, J. E., & Shekelle, C. D. (1993). The AGOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, *31*, 471-481.

Wolke, M., B. M., Selzer, B., Fink, J., Florschütz, R., Schell, G., & Merzhausen, B. (1994). Graft-versus-host disease after bone marrow transplantation in cancer patients. *Cancer Treatment Reviews*, *20*(3), 181-201.

Wolke, D. (1991). *Das Wächler-Jahrbuch Intelligente Entscheidungen*. San Antonio, TX: The Psychological Corporation.

Wong, C. S. (1992). Depression and stress in organ donors: A review of the literature. *Psychological Bulletin*, *111*, 475-491.

Wright, J. R. (1994). Functional status and quality of life of patients after allogeneic bone marrow transplantation. *Bone Marrow Transplantation*, *13*(suppl. 4), 621-622.

Wright, J. R., Cutrow, B., Baker, F., Zelen, J., & Friedman, S. (1991). Social adaptation in survivors of bone marrow transplantation. *Bone Marrow Transplantation*, *6*, 181-189.

Wright, J. R., Cutrow, B., Baker, F., & Friedman, S. (1991). Health functional status and employment of adult survivors of bone marrow transplantation. *Annals of Internal Medicine*, *114*, 111-119.

Wright, D. L., Wolke, D. E., Roney, J. J., & Lindbeck, J. (1990). Adjustment of adult bone marrow transplant recipient long-term survivors. *Transplantation*, *51*, 474-484.

Wright, J. R., Jorvik, E. D., Baker, F., Wright, J. R., & Cutrow, B. (1991). The family: the other side of bone marrow transplantation. *Journal of Psychosocial Oncology*, *25*, 33-48.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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